UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,692	10/07/2003	Benjamin G. Davis	GRT/117-480	7864

23117 7590 09/26/2008

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
09/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,692	DAVIS, BENJAMIN G.	
	Examiner	Art Unit	
	IQBAL H. CHOWDHURY	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/22/08; 2/8/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,16,17,19 and 41* is/are pending in the application.

4a) Of the above claim(s) *27-32,44 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,5-15, 16,17,19 23 and 41* is/are rejected.

7)☒ Claim(s) *43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

Claims 1-17, 19-21, 23, 27-32 and 38-45 are currently pending in this application.

Since, claims submitted on 7/8/2008 and 2/8/2008 are identical, the Examiner will consider claim submitted on 2/8/2008 only.

In response to a previous Office action, a final action (mailed on December 28, 2007), Applicants filed an amendment on February 8, 2008, amending claims 1, 5-7, 10, 13, 17, 21, 27, 30, 39 and 41-45, canceling claims 18 and 22 is acknowledged. Claims 27-32 and 44-45 remain withdrawn, and claims 24-26 and 33-37 remain cancelled.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 22, 2008 has been entered.

Claims 1-17, 19-21, 23 and 38-43 are under consideration and are present for examination.

Applicants' arguments filed on 2/8/2008 and 7/8/2008 have been fully considered but are not deemed persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

New-Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-4, 16-17, 19, and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is indefinite in the recitation of "SEQ ID NO: 2 mutated with at least one or more mutations in an amino acid residue selected from the group consisting of W433, E432 and M439", which is confusing. It is not clear to the Examiner whether the mutations are limited to mutations at residues W433, E432 and M439 of SEQ ID NO: 2 only or including others. The rejection can be overcome by rewriting the phrase as "SEQ ID NO: 2 mutated at an amino acid residue or residues selected from the group consisting of W433, E432 and M439 and combinations thereof". Accordingly, claims 3-4, 16-17, 19, and 41 are also rejected, as they are dependent on claim 1.

Claims 1-4, 16-17, 19-21, 38-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is indefinite in the recitation "a polypeptide having β-glycosidase activity … said polypeptide having an optional mutation of a catalytic nucleophilic residue of active site", which is confusing. The specification teaches that a polypeptide having a mutation at catalytic nucleophilic residue at active site lacks beta-glycosidase enzymatic activity. The specification at page 10, line 1-6, teaches that mutating a nucleophilic residue at the active site of glycosidase enzyme results in converting a glycosidase enzyme to a glycosynthase

enzyme and that the variant enzyme lacks hydrolase activity. Accordingly, claims 3-4, 16-17, 19, and 41 are also rejected, as they are dependent on claim 1.

Maintained-Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Previous rejection of Claims 1-4, 5-15, 16-17, 19-21, 23 and 38-42 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4, 5-15, 16-17, 19-21, 23 and 38-42 are directed to a modified polypeptide having beta-glycosidase activity, comprising (a) the amino acid sequence of SEQ ID NO:2 mutated with at least one or more mutations in an amino acid residue selected from the group consisting of W433, E432 and M439; (b) the amino acid sequence of a family 1 glycosyl hydrolase, comprising any mutation at least at an amino acid residue corresponding to at least one of W433, E432 and M439; and (c) a variant of (a) having beta-glycosidase activity and comprising any mutation in an amino acid residue corresponding to at least one of W433, E432 and M439 of SEQ ID NO:2, wherein said

variant has at least 95% identity to SEQ ID NO:2 over the entire length of the sequence of SEQ ID NO:2 and the polypeptide having an optional mutation of a catalytic nucleophilic residue of the active site. Claim 41 recites the polypeptide of claim 1, wherein said polypeptide comprising an amino acid sequence selected from: (a) the amino acid sequence of SEQ ID NO:2 comprising a mutation in at least one of W433, E432 and M439; and (b) the amino acid sequence of a family 1 glycosyl hydrolase, comprising a mutation at an amino acid residue corresponding to at least one of W433, E432 and M439 of SEQ ID NO:2; wherein said polypeptide further comprises a mutation of a catalytic nucleophilic residue of the active site. The rejection was explained in the previous Office Action.

Applicants argue that the specification teaches a representative number of species within the claimed genus and the claims are directed to polypeptides having at least β-glycosidase activity. This recitation, along with corrective amendments to clarify the nature of the mutations in the polypeptide as compared to the amino acid sequence of SEQ ID NO:2, complies with the written description requirement because such modified polypeptides were in the possession of Applicant when this application was filed.

Applicant's arguments and amendments to claims have been fully considered but are not deemed persuasive to overcome the rejection on written description issues. Examiner acknowledges amendment to the claims, however the amendment does not give enough structural feature of any mutation in SEQ ID NO: 2, i.e. unlimited number of mutations in SEQ ID NO: 2 including at least one of W433, E432 and M439 due to the

recitation "the amino acid sequence of SEQ ID NO: 2 mutated with at least one or more mutations", and "the amino acid sequence of a family 1 glycosyl hydrolase mutated at an amino acid residue corresponding to at least one of W433, E432 and M439" as well as a mutation of a catalytic nucleophilic residue of the active site of the modified polypeptide having glycosidase enzymatic activity, which is required for fulfilling written description requirements. Claim 1 part (a) and (b) does not have any structural feature at all, which is very broad. The term "SEQ ID NO: 2 mutated with at least one or more mutations" includes mutation of any number of amino acid residues of SEQ ID NO:2 or the family 1 glycosyl hydrolase in addition to the alteration at the recited the amino acid residues, i.e. W433, E432 and M439, and results in any structure of said modified protein. Furthermore, "any mutation of a catalytic nucleophilic residue of the active site of the modified polypeptide of SEQ ID NO: 2 having glycosidase enzymatic activity" is not described as it is in fact directly contradictory to the teaching of the specification. Indeed, the specification at page 10, line 1-6, teaches that mutating a nucleophilic residue at the active site of glycosidase enzyme results in converting a glycosidase enzyme to a glycosynthase enzyme and said mutant protein does not have any glycosidase activity, which is inconsistent to the claimed invention and such recitation makes the claim lack of necessary glycosidase functional feature. Therefore, one of skill in the art would not know the specific structure function correlation of the modified polypeptide to practice the claimed invention. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction

to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of species disclosed. For inventions in an unpredictable art, adequate written description of a genus, which embraces widely variant species, cannot be achieved by disclosing only one species within the genus. The specification teaches a single representative species of SEQ ID NO: 2 and few mutant proteins having few mutations. The genus of modified polypeptide of SEQ ID NO: 2 having any mutation at position W433, E432 and M439 is structurally diverse as it broadly encompasses many mutants and variants comprising beta-glycosidase activity having different structures. As such, the disclosure is solely of functional features coupled with minor structural feature that may or may not present in all members of the genus is insufficient to be representative of the attributes and features of the entire genus (structure and function). Claims 38-42 are included in this rejection because of the recitation “said polypeptide having an

optional mutation of a catalytic nucleophilic residue of the active site" in claims 1 and 41, upon which claims 38-40 and 42 depend. The specification at page 10, line 1-6, teaches that mutating a nucleophilic residue at the active site of glycosidase enzyme results in converting a glycosidase enzyme to a glycosynthase enzyme and said mutant protein does not have any glycosidase activity, which is inconsistent to the claimed invention and such recitation makes the claim lack of necessary glycosidase functional feature.

Therefore, the rejection is maintained.

Maintained - Claim Rejections - 35 U.S.C. § 112

Previous rejection of Claims 1-4, 5-15, 16-17, 19-21, 23 and 38-42 under 35 U.S.C. 112, first paragraph, on enablement requirement is maintained. This rejection has been described at length in previous Office Action. The rejection is maintained for the following reasons.

Applicants argue that the specification enables the skilled artisan to practice the claimed invention. The claims are directed to polypeptides having at least β-glycosidase activity. This recitation, along with corrective amendments to clarify the nature of the mutations in the polypeptide as compared to the amino acid sequence of SEQ ID NO:2, complies with the enablement requirement because it would not require undue experimentation to make and use such modified polypeptides.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims on scope of the enablement issues. The specification, while being enabling for a modified polypeptide of beta-glycosidase of

SEQ ID NO: 2 having beta-glycosidase activity comprising a mutation at M439 (methionine at 439 position) to C439 i.e. M439C, does not reasonably provide enablement for any variant polypeptide having any number of mutations at any positions of SEQ ID NO: 2 or any polypeptide having beta-glycosidase activity and an optional mutation of a catalytic nucleophilic residue of the active site of SEQ ID NO: 2 or family 1 glycosyl hydrolase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Amended claims still read on any modified polypeptide comprising any number of mutations in SEQ ID NO: 2 including at least one of W433, E432 and M439 of SEQ ID NO: 2 having glycosidase activity (claims 1, 5 and claims 2-4, 6-17, 19-21, 23 and 41 dependent thereon) and "a polypeptide having beta-glycosidase activity and any mutation of a catalytic nucleophilic residue of the active site" of the polypeptide because such mutation will make the polypeptide have no beta-glycosidase activity (claim 1-4, 16, 17, 19-21, and 38-42). The term "SEQ ID NO: 2 mutated with at least one or more mutations" includes mutation of any number of amino acid residues of SEQ ID NO:2 or the family 1 glycosyl hydrolase in addition to the alteration at the recited the amino acid residues, i.e. W433, E432 and M439, which results in any structure of said modified protein. In addition, the recitation "the polypeptide having an optional mutation of a catalytic nucleophilic residue of the active site", would make the enzyme having no beta-glycosidase activity, which is contradictory to the claimed invention. One of ordinary skill in the art would not practice the claimed invention without knowing the

specific structural feature of claimed modified polypeptide correlated with functional feature, which would require undue experimentation. As mentioned in the previous Office Actions, Claims are so broad as to encompass a modified polypeptide having beta-glycosidase activity comprising any number of mutations at any position of SEQ ID NO: 2, wherein a mutation in at least one or more of positions of W433, EE432 and in M439 is included or an enzyme having family 1 glycosyl hydrolase activity comprising any mutations, wherein a mutation in at least one or more of the positions of W433, EE432 and in M439 is included or any mutation of a catalytic nucleophilic residue of the active site" of the polypeptide having beta-glycosidase activity.

The scope of the claimed invention is substantially broad in the context of 1) any mutation at any positions of SEQ ID NO: 2 (part (a)) having beta-glycosidase activity; or 2) any mutation at any positions of a family 1 glycosyl hydrolase activity, which includes many mutants or variants (part (b)).

The specification clearly requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of glycosyl hydrolase have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification. As previously stated the applicants have not

provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a modified enzyme of SEQ ID NO: 2 having any number of mutations including at positions W433, E432 and M439 of SEQ ID NO: 2 having family 1 glycosyl hydrolase activity because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting beta glycosidase activity; (B) the general tolerance of glycosyl hydrolase polypeptides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues of the polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Claims 38-42 are included in this rejection because of the recitation "said polypeptide having an optional mutation of a catalytic nucleophilic residue of the active site" in claims 1 and 41, upon which claims 38-40 and 42 depend. The specification at page 10, line 1-6, teaches that mutating a nucleophilic residue at the active site of glycosidase enzyme results in converting a glycosidase enzyme to a glycosynthase enzyme and said mutant protein does not have any glycosidase activity, which is inconsistent to the claimed invention and such recitation makes the claim lack of necessary glycosidase functional feature for which the specification provides absolutely no guidance whatsoever.

Therefore, the rejection is maintained.

Conclusion

Claims 1-17, 19-21, 23, 27-32 and 38-45 are pending.

Claims 27-32 and 44-45 are withdrawn.

Claim 43 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 1-4, 5-15, 16-17, 19, 23 and 38-42 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Iqbal Chowdhury, PhD Patent Examiner
Art Unit 1652 (Recombinant Enzymes)
US Patent and Trademark Office
Remsen Bldg., Rm. 2B69, Mail Box. 2C70
Ph. (571)-272-8137, Fax. (571)-273-8137

/I. H. C./
Examiner, Art Unit 1652

/Rebecca E. Prouty/
Primary Examiner,
Art Unit 1652